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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/836,439	04/17/2001	Therese de Bizemont	017753-154	5851

21839 7590 12/24/2002

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EXAMINER
SCHNIZER, RICHARD A

ART UNIT	PAPER NUMBER
1635	16

DATE MAILED: 12/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/836,439	Bizemont
Examiner	**Art Unit**
Richard Schnizer	1635

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 24, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☐ Claim(s) _____ is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-39* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants election with traverse of group I, claims 1-21 in paper No. 15, filed 10/24/02 is acknowledged.

After consideration of Applicant's traversal and request for reconsideration, the previous restriction requirement is withdrawn in favor of the following requirement.

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-18, 20, 21, 30, and 39 drawn to methods of delivering an oligonucleotide for reversion of a K296E mutation in human RP1 *in vivo* to cells of an animal by iontophoresis, classified in class 435, subclass 455.

II. Claims 1-18, 20, 21, 30, and 39 drawn to methods of delivering an oligonucleotide for reversion of a R677STOP mutation in human RP1 *in vivo* to cells of an animal by iontophoresis, classified in class 435, subclass 455.

III. Claims 1-17, 19, 20, 21, and 31 drawn to methods of delivering an oligonucleotide for induction of a K296E mutation in mouse RP1 *in vivo* to cells of an animal by iontophoresis, classified in class 435, subclass 455.

IV. Claims 1-17, 19, 20, 21, and 31 drawn to methods of delivering an oligonucleotide for induction of a E348STOP mutation in mouse RP1 *in vivo* to cells of an animal by iontophoresis, classified in class 435, subclass 455.

V. Claims 1-17, 19, 20, 21, and 31 drawn to methods of delivering an oligonucleotide for reversion of a K296E mutation in mouse RP1 *in vivo* to cells of an animal by iontophoresis, classified in class 435, subclass 455.

VI. Claims 1-17, 19, 20, 21, and 31 drawn to methods of delivering an oligonucleotide for reversion of a E348STOP mutation in mouse RP1 *in vivo* to cells of an animal by iontophoresis, classified in class 435, subclass 455.

VII. Claims 22-24 and 33, drawn to methods of treating inherited retinopathy in an animal by delivering by iontophoresis a chimeric oligonucleotide to cells of the animal, classified in class 514, subclass 44.

VIII. Claims 22, 23 and 34, drawn to methods of treating ocular neovascularization in an animal by delivering by iontophoresis a chimeric oligonucleotide to cells of the animal, classified in class 514, subclass 44.

IX. Claim 25 drawn to a method of making an animal model by administering by iontophoresis a chimeric oligonucleotide to cells of the animal, classified in class 800, subclass 9.

X. Claims 27, 28, 32, and 37, drawn to chimeric oligonucleotides for reverting a C to A transversion at codon 347 of a gene encoding murine cGMP phosphodiesterase beta subunit, classified in class 536, subclass 23.1.

XI. Claims 29 and 38, drawn to a chimeric oligonucleotide capable of inducing a nonsense mutation in DNA encoding murine or human transcription factor HIF1alpha such that the subsequently encoded protein is nonfunctional, classified in class 536, subclass 23.1.

XII. Claims 35 and 36, drawn to an animal model comprising a mutation in the RP1 gene, classified in class 800, subclass 9.

Claims 1-17, 20, and 21 are generic to a plurality of patentably distinct inventions listed as groups I-VI. Claims 18, 30, and 39 are generic to a plurality of patentably distinct inventions listed as groups I and II. Claims 19 and 31 are generic to a plurality of patentably distinct inventions listed as groups III-VI. Claims 22 and 23 are generic to a plurality of patentably distinct inventions listed as groups VII and VIII. If any of these groups is elected, the claims will be examined only to the extent that they are defined by the elected group.

Inventions I-VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the methods lead to different results and modes of operation, i.e. unrelated changes in nucleic acid sequence

due to introduction of structurally distinct oligonucleotides. The specification does not disclose the methods as capable of use together, and they have different effects as noted above.

Inventions I-VI are related to inventions VII-IX as a combinations and subcombinations. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the method of group I need not be used for disease treatment or for making an animal model, rather it may be used for studying gene function in vivo. The subcombinations have separate utilities as listed, i.e. for disease treatment and for making animal models.

Inventions X and XI are unrelated to Inventions I-VI. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the oligonucleotides of groups X and XI cannot be used in the methods of Inventions I-VI because these methods require structurally and functionally distinct oligonucleotides.

Inventions I, II, V and VI are unrelated to invention XII. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the methods of Inventions I, II, V and VI do not require or produce the animal model

of Invention XIII. The specification does not disclose the methods as capable of use together with the product.

Inventions III and IV are related to invention XII as processes of making a product and a product made by the processes. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the animal model of group XII can be made through standard transgenic technology by microinjection of an altered gene into an ES cell followed by selection for homologous recombinants comprising the desired gene replacement and RP1 mutation.

The inventions of groups VII and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the two methods lead to different results, i.e. treatment of inherited retinopathy and treatment of neovascularization, i.e. treatment of separate and distinct diseases. As such the methods require different materials, and have different modes of operation and different effects. The specification does not disclose the methods as capable of use together.

The inventions of groups VII and VIII are unrelated to the invention of group IX. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP §

806.04, MPEP § 808.01). In the instant case the methods lead to different results, i.e. disease treatment (inventions VII and VIII) and the development of an animal model (invention IX). The specification does not disclose the methods as capable of use together, and they have different effects as noted above.

The oligonucleotides of inventions X and XI are related to the disease treatment methods of inventions VII and VIII because the oligonucleotides could be used in a disease treatment method. However, the inventions are distinct because the oligonucleotides could be used in various patentably distinct methods such as in vitro mutagenesis. Furthermore, other oligonucleotides could be used in disease treatment.

The animal model of invention XII is related to the method invention VII because the animal model could be used to test the method. The inventions are distinct because the animal model could be used for other patentably distinct methods such as the study of the histopathology of retinopathy.

The animal model of RP1 mutation of invention XII is unrelated to the method of group VIII. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the animal model of RP1 mutation is not produced by any method of treating neovascularization, and is not disclosed as being capable of use in the method.

The method of making an animal model of invention IX is related to the oligonucleotides of groups X and XI as a method of use is related to products. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the products can be used in materially different processes such as the induction of mutations in vitro.

Invention IX is related to invention XII as processes of making a product and a product made by the processes. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the animal model of group XII can be made through standard transgenic technology by microinjection of an altered gene into an ES cell followed by selection for homologous recombinants comprising the desired gene replacement and RP1 mutation.

Inventions X and XI are unrelated. Invention X is drawn to a specific oligonucleotide for reverting a C to A transversion at codon 347 of murine cGMP phosphodiesterase, whereas invention XI is directed to an oligonucleotide for inducing a nonsense mutation in a HIF1 alpha transcription factor gene. The products are structurally and functionally distinct, and are not disclosed as capable of use together in the same method.

Inventions X and XI are unrelated to the animal model of Invention XII. The oligonucleotides of Inventions X and XI cannot be used to make an animal model of comprising an RP1 mutation because they are designed for the purpose of modifying cGMP phosphodiesterase of HIF alpha genes.. Thus the oligonucleotides have modes of operation and effects that are unrelated to an animal model comprising a mutation in an RP1 gene.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification and their recognized divergent subject matter, and because each invention requires a separate, non-coextensive search, restriction for examination purposes as indicated is proper.

Claim 1 link(s) inventions I-VI. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 1. Further, claim 22 link(s) inventions VII and VIII. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 1 or claim 22. Upon the allowance of a linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is

withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 103-306-5441. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is usually in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Leguyader, can be reached at 703-308-0447. The FAX numbers for art unit 1632 are 703-308-4242, and 703-305-3014. Additionally correspondence can be transmitted to the following RIGHTFAX numbers: 703-872-9306 for correspondence before final rejection, and 703-872-9307 for correspondence after final rejection.

Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 703-305-3413.

Richard Schnizer, Ph.D.

JEFFREY SIEW
PRIMARY EXAMINER
12/23/02